REMARKS

Applicant wishes to express his appreciation for the courtesies extended Applicant's representatives, Joseph Mahoney, Dr. Gary Ringham, and Sandy Faulkner, during the December 6, 2001 interview with the Examiner and Examiner Russell Travers.

In the Office Action dated June 5, 2002, claims 33, 35, 36, 41, 42, 45, 48, 49, 57-59, 62, 64, 75-83, 88-93, 97-99 and 101-210, were rejected. Upon entry of this Amendment, claims 33, 35, 36, 41, 42, 45, 48, 49, 57-59, 62, 64, 75-83, 88-93, 97-99 and 101-210 are pending and under consideration in the present application. The Examiner's withdrawal of the 35 U.S.C. § 112, second paragraph, rejection of claims 35, and 41-43 is acknowledged.

Applicant respectfully submits that no new matter has been added by way of this amendment.

I. Rejections under 35 U.S.C. § 103

Claims 33, 35, 36, 41, 42, 45, 48, 49, 57-59, 62, 64, 75-83, 88-93, 97-99 and 101-210 were rejected under 35 U.S.C. § 103(a) as being unpatentable over Mak *et al.* (WO 99/24041-A1) and Heiber, *et al.* (WO 93/25168), and Omar (U.S. Patent No. 5,730,987) and Moreland *et al.* (Life Sciences 1998, 62(2), 309-318) in view of Allen (WO 96/27372-A1). The Office Action stated that:

> It would have been obvious to a person of ordinary skill in the art at the time the invention was made to employ the particular steroid, testosterone, C1-C4 alcohol, and the particular penetration enhancer, C8-C22 fatty acid and isopropyl myristate in a method for improving the efficacy of the composition herein useful for treating erectile dysfunction in a male who may by an eugonadal, and to further add the phosphodiesterase type 5 inhibitor, sildenafil or yohimbine HCl to the composition, and optimize the effective amounts of active ingredients in the composition.

Applicant respectfully traverses this rejection in light of the amended claims and the remarks presented herein.

It is well established that the burden of establishing a *prima facie* case of obviousness lies with the Examiner. In determining obviousness, one must focus on the invention as a whole. *See* In re Keuhl, 475 F.2d 658, 177 U.S.P.Q. 250 (C.C.P.A 1973); Symbol Technologies Inc. v. Opticon Inc., 19 USPQ 2d 1241, 1246 (Fed. Cir. 1991). Thus, "[i]n determining the difference between the prior art and the claims, the question under 35 U.S.C. 103 is not whether the differences themselves have been obvious, but whether the claimed invention as a whole would have been obvious. *See* MPEP 2141.02 (emphasis in original). Thus, patentability of a method of use claim hinges on the patentability of the underlying composition, and even if the steps recited in the methods are well known, so long as the method uses a patentable material, it is unobvious. *See* In re Pleuddemann, 910 F.2d 283, 15 U.S.P.Q.2d 1782 (Fed. Cir. 1990).

In view of the amendments and remarks presented herein, Applicants respectfully submit that a *prima facie* case of obviousness has not been established. As taught by the present invention, in one aspect, Applicant claims a method for improving the efficacy of a pharmaceutical useful for treating erectile dysfunction in a male subject by percutaneously administering a pharmacologically effective amount of a composition consisting essentially of:

a) about 0.5 % to about 10 % testosterone;

b) about 30 % to about 98 % alcohol selected from the group consisting of ethanol, and isopropanol;

c) about 0.1 % to about 5 % isopropyl myristate;

d) about 1 % to about 5 % sodium hydroxide; and

e) about 0.1 % to about 5 % gelling agent.

In rejecting the present claimed invention under 35 U.S.C. § 103, the Office Action stated that:

> Since all composition components herein are known to be useful to treat male erectile dysfunction, it is considered *prima facie* obvious to combine them into a single composition useful for the very same purpose.

(emphasis added). As stated above, however, the question under 35 U.S.C. § 103 is not whether the differences themselves would have been obvious, but whether the claimed invention as a whole would have been obvious. In this case, the present claimed method utilizes a novel and nonobvious composition that is subject to a notice of allowance in the parent case, U.S. Patent Application serial No. 09/651,777 ("the '777 application"). Therefore, the basis for this obviousness rejection does not take into consideration the claimed invention as a whole, but looks only at the components themselves. Additionally, Applicant acknowledges that the Office Action stated that:

> The prior art does not expressly disclose a method of improving the efficacy of a pharmaceutical useful for treating erectile dysfunction in a male who may be an eugonadal comprising the particular steroid, testosterone, C_1-C_4 alcohol, and the particular penetration enhancer, isopropyl myristate, and the effective amounts of active ingredient in the composition.

Applicant therefore contends that the 35 U.S.C. § 103(a) rejection of the present claims is improper.

Applicant also contends that the use of In re Kerkhoven, 626 F.2d 846 (CCPA 1980), in supporting the rejection of the present claims is misplaced. In re Kerkhoven holds that:

> It is prima facie obvious to combine two compositions each of which is taught by the prior art to be useful for the same purpose, in order to form a third composition which is to be used for the very same purpose.

Id. at 850 (emphasis added). As acknowledged in the parent case, the '777 application, the novel and unobvious composition as claimed in the present case is not taught by the prior art. "Obviousness cannot be predicated on what is not known at the time an invention is made, even if the inherency of a certain feature is later established." MPEP 2141.02 (emphasis added). Thus, the present invention taken as a whole cannot be combined without using

hindsight because the novel and unobvious composition of the present invention was not taught by the prior art.

In the references cited by the Examiner, Omar teaches oral administration of a powdered composition of lyophilized roe and powdered extract of *Gingo biloba*. It also mentions that testosterone may be administered by injection, orally or by buccal tablets for hypogonadism. However, Omar does not teach or suggest the present invention of improving the efficacy of a pharmaceutical administered to a male subject useful for treating erectile dysfunction by percutaneously administering the present claimed composition.

Mak *et al.* teach transdermal and topical delivery of testosterone, a C1-C4 alcohol and a penetration-enhancing agent. Mak *et al.* also do not teach or suggest a method of improving the efficacy of a pharmaceutical administered to a male subject useful for treating erectile dysfunction by percutaneously administering the present claimed composition.

Heiber *et al.* teach the use of varying amounts of glycerin in a composition containing testosterone, a C2 or C3 alcohol, for example, ethanol, glycerol monoleate, and methyl laureate, useful in methods of moderating and maintaining transdermal drug delivery to the derma/mucosa at a relatively sustained rate over the duration of the application to either an application or afflicted situs. Heiber *et al.* do not teach or suggest a method of improving the efficacy of a pharmaceutical administered to a male subject useful for treating erectile dysfunction by percutaneously administering the present claimed composition.

Moreland *et al.* teach oral administration of sildenafil for the treatment of male erectile dysfunction. Moreland *et al.* also do not teach or suggest improving the efficacy of a pharmaceutical administered to a male subject useful for treating erectile dysfunction by percutaneously administering the present claimed composition.

Allen teaches a water-based topical cream containing the vasodilator nitroglycerin (which is not a hormone that plays a role in erections) for the treatment of male erectile

dysfunction. Allen does not teach or suggest improving the efficacy of a pharmaceutical administered to a male subject useful for treating erectile dysfunction by percutaneously administering the present claimed composition.

In the 35 U.S.C. §103(a) rejection of the present claims, the Office Action has cited no pertinent reference showing or suggesting to one of ordinary skill in the art the present invention as a whole. Reconsideration and withdrawal of this 35 U.S.C. § 103(a) rejection is respectfully requested.

II. Conclusion

With entry of the above Amendment and in view of the foregoing remarks, it is respectfully submitted that claims 33, 35, 36, 41, 42, 45, 48, 49, 57-59, 62, 64, 75-83, 88-93, 97-99 and 101-210 are in condition for allowance.

None of Applicant's amendments or cancellations are to be construed as dedicating any such subject matter to the public, and Applicant reserves all rights to pursue any such subject matter in this or a related patent application. The amendments are made solely to expedite prosecution.

Submitted below is separate page titled "Version with Marking to Show Changes Made to the Claims," showing a marked-up copy of prior pending claims.

It is respectfully submitted in view of the foregoing Amendment and Remarks that all of the objections and rejections in the Office Action dated June 5, 2002 have been overcome and should be withdrawn. Applicants respectfully request early and favorable notification to that effect.

The Examiner is invited to call Applicant's undersigned attorney at (312) 701-8775

for questions and to expedite prosecution.

Respectfully submitted,

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Version with Marking to Show Changes Made to the Claims

101. (Amended) A method for improving the efficacy of a pharmaceutical useful for treating erectile dysfunction in a male subject, comprising:

percutaneously administering to an area of skin of the subject a pharmacologically [pharmaceutically] effective amount of a composition consisting essentially of [comprising]:

a) about 0.5 % to about 10 % testosterone;

b) about 30 % to about 98 % alcohol selected from the group consisting of ethanol, and isopropanol;

c) about 0.1 % to about 5 % isopropyl myristate;

d) about 1 % to about 5 % sodium hydroxide; and

e) about 0.1 % to about 5 % gelling agent;

wherein the percentages are weight to weight of the composition.

102. (Amended) A method for improving the efficacy of a pharmaceutical useful for treating erectile dysfunction in a male subject, comprising:

percutaneously administering to the subject a pharmacologically [pharmaceutically] effective amount of a composition consisting essentially of [comprising]:

a) about 0.5 % to about 10 % testosterone;

b) about 30 % to about 98 % alcohol selected from the group consisting of ethanol, and isopropanol;

c) about 0.1 % to about 5 % isopropyl myristate;

d) about 1 % to about 5 % sodium hydroxide; and

e) about 0.1 % to about 5 % gelling agent; and

administering the pharmaceutical to the subject;

wherein the amount of the composition administered to the subject is sufficient to achieve an erection for sexual intercourse in the subject; and the percentages are weight to weight of the composition.

149. (Amended) A method for improving the efficacy of a pharmaceutical useful for treating erectile dysfunction in a male subject, comprising:

percutaneously administering to the subject a pharmacologically [pharmaceutically] effective amount of a composition consisting essentially of [comprising]:

a) about 0.5 % to about 10 % testosterone;

b) about 30 % to about 98 % alcohol selected from the group consisting of ethanol, and isopropanol;

c) about 0.1 % to about 5 % isopropyl myristate;

d) about 1 % to about 5 % sodium hydroxide; and

e) about 0.1 % to about 5 % gelling agent; and

administering the pharmaceutical to the subject;

wherein the amount of the composition administered to the subject is sufficient to achieve hormonal steady state levels of testosterone in the subject; and the percentages are weight to weight of the composition.